FIG. 1

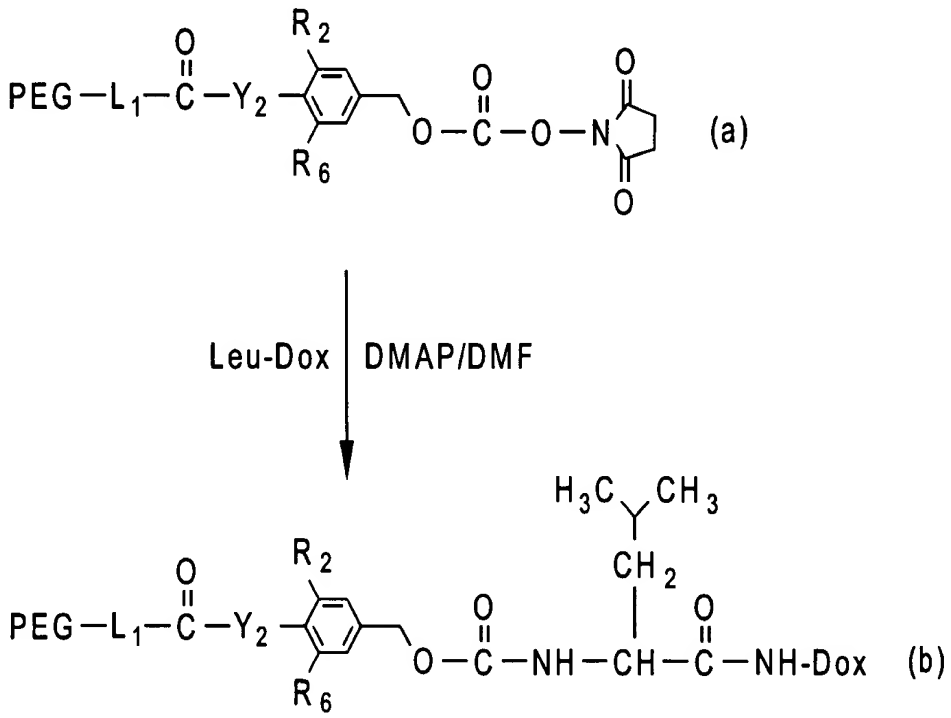

PEG—L1—C—Y2
R2
R6
O—C—O—N
(a)
Leu-Dox
DMAP/DMF
H3C CH3
CH2
O—C—NH—CH—C—NH-Dox
(b)

FIG. 2A

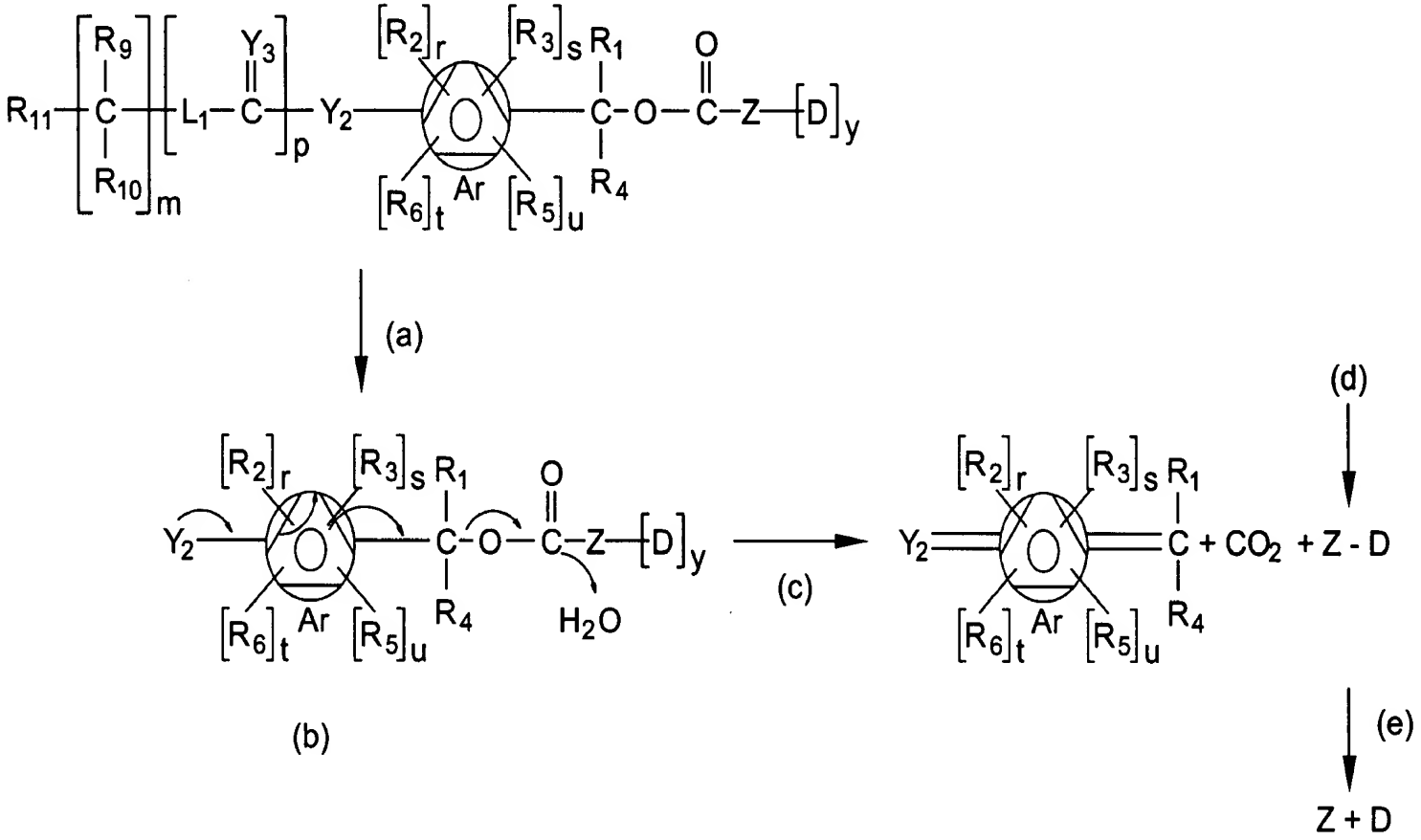


FIG. 2B

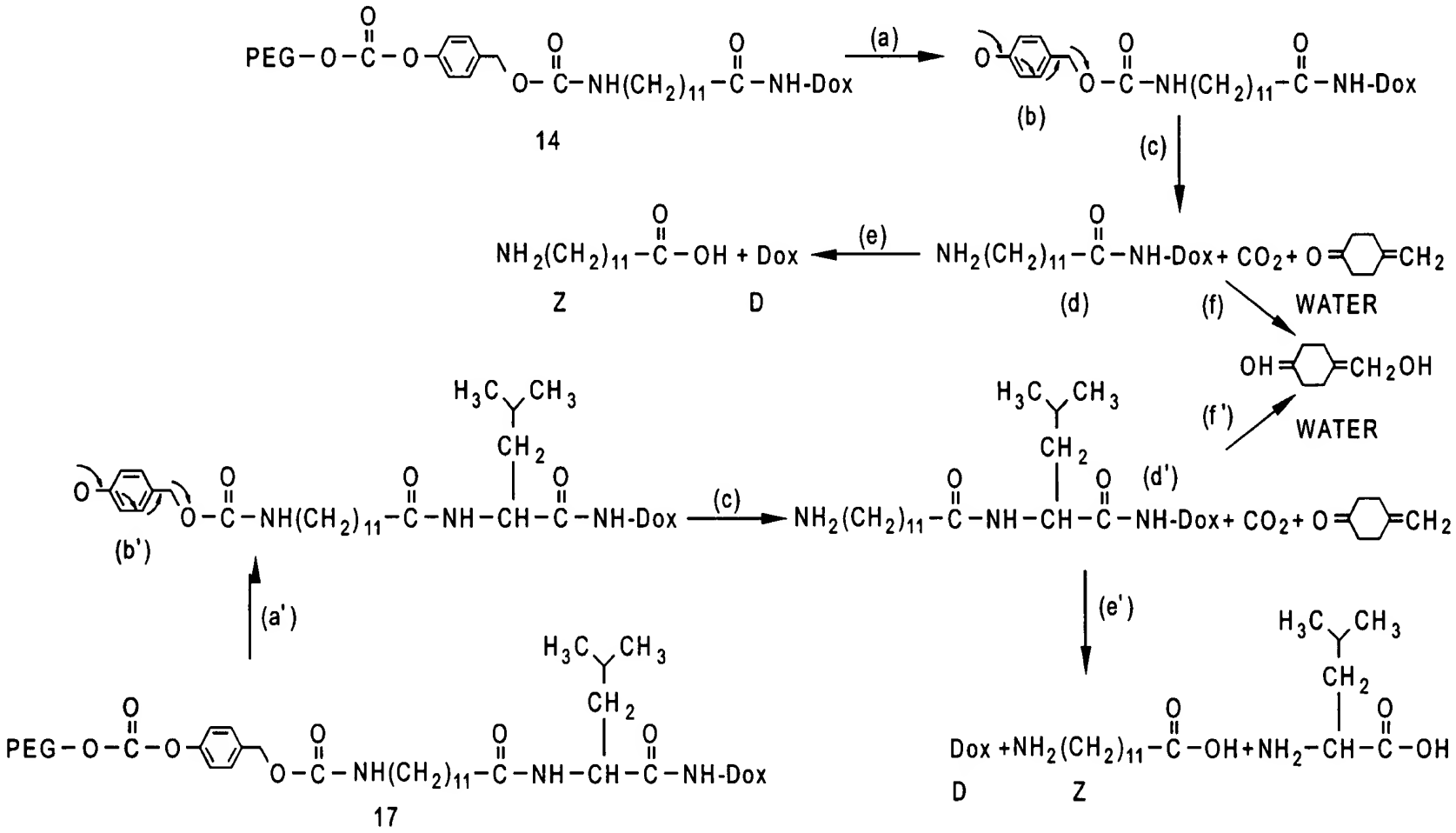

PEG-O-C-O
O-C-NH(CH2)11-C-NH-Dox
14
(a)
(b)
(c)
NH2(CH2)11-C-OH + Dox
Z
D
(e)
NH2(CH2)11-C-NH-Dox + CO2 + O=CH2
(d)
(f)
WATER
OH=CH2OH
(f')
WATER
(b')
(c)
(d')
(a')
(e')
17
Dox + NH2(CH2)11-C-OH + NH2-CH-C-OH
D
Z

FIG. 3

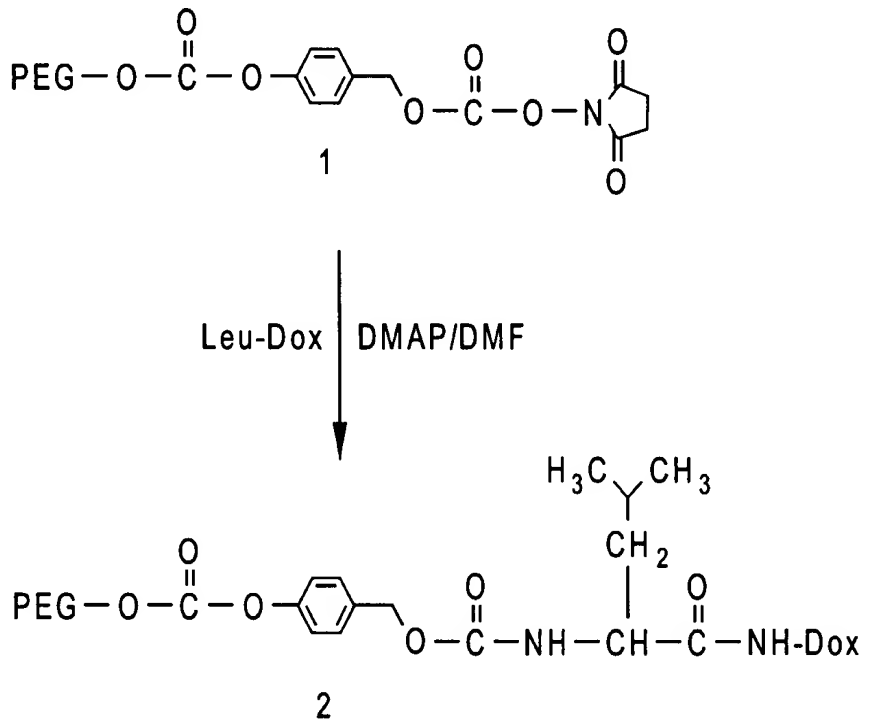

PEG—O—C—O
O—C—O—N
1
Leu-Dox
DMAP/DMF
H3C CH3
CH2
PEG—O—C—O
O—C—NH—CH—C—NH-Dox
2

FIG. 4

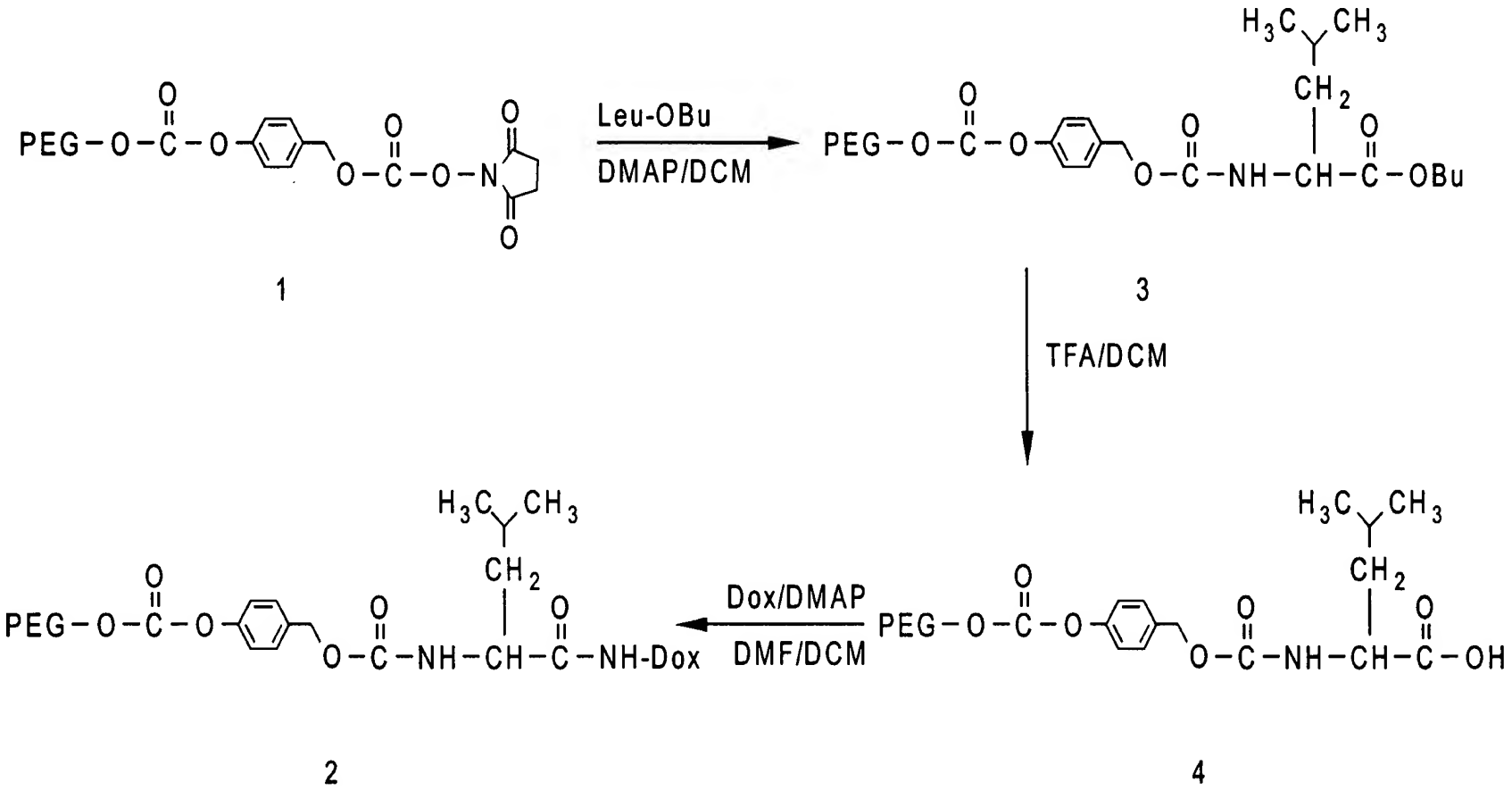
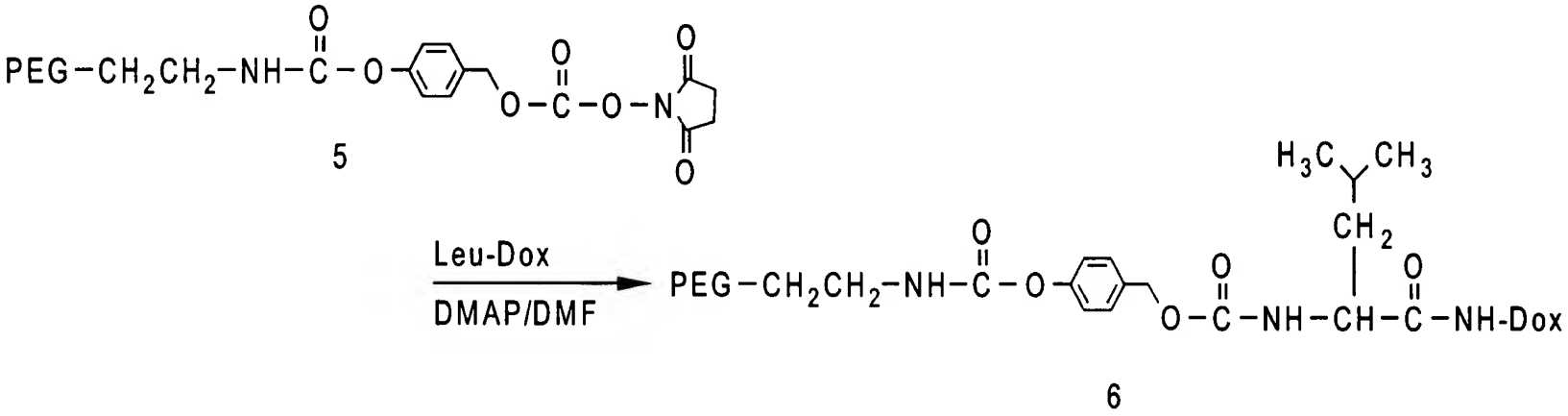

PEG-O-C-O
O-C-O-N
Leu-OBu
DMAP/DCM
O-C-NH-CH-C-OBu
H3C CH3
CH2
1
3
TFA/DCM
Dox/DMAP
DMF/DCM
O-C-NH-CH-C-NH-Dox
O-C-NH-CH-C-OH
2
4

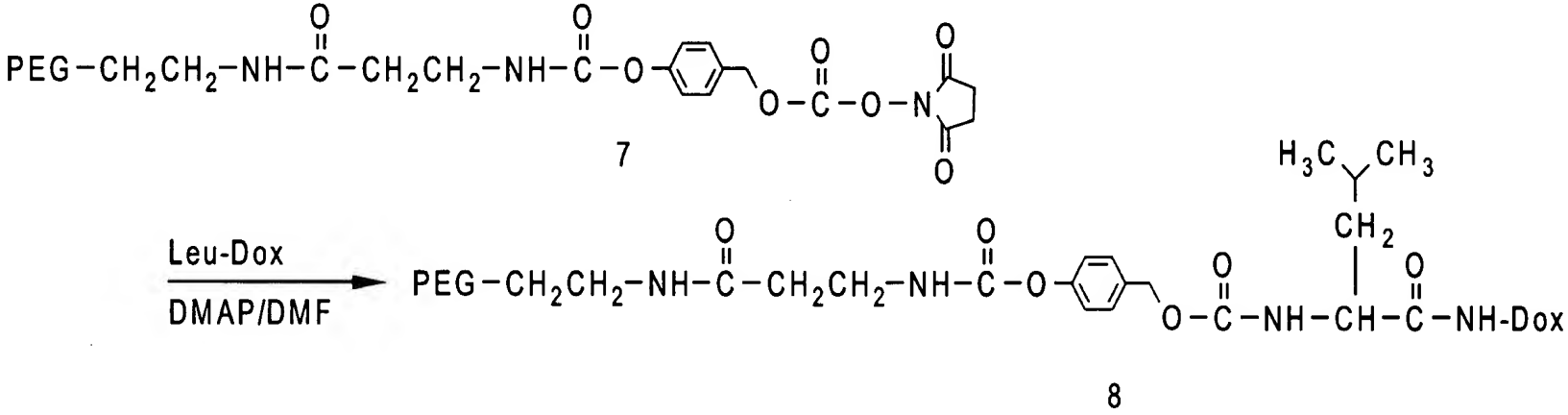
FIG. 5



5

6

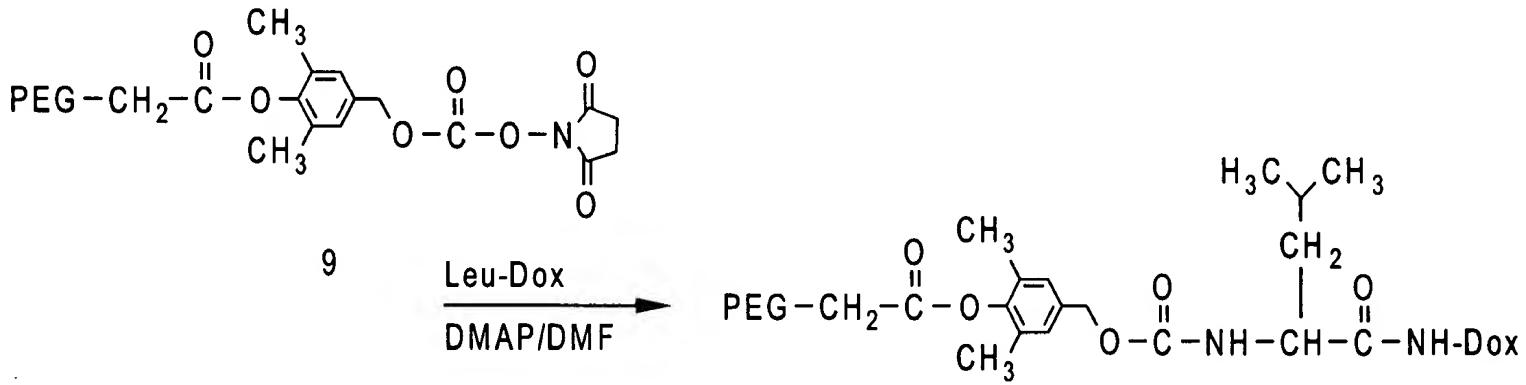
FIG. 6



7

8

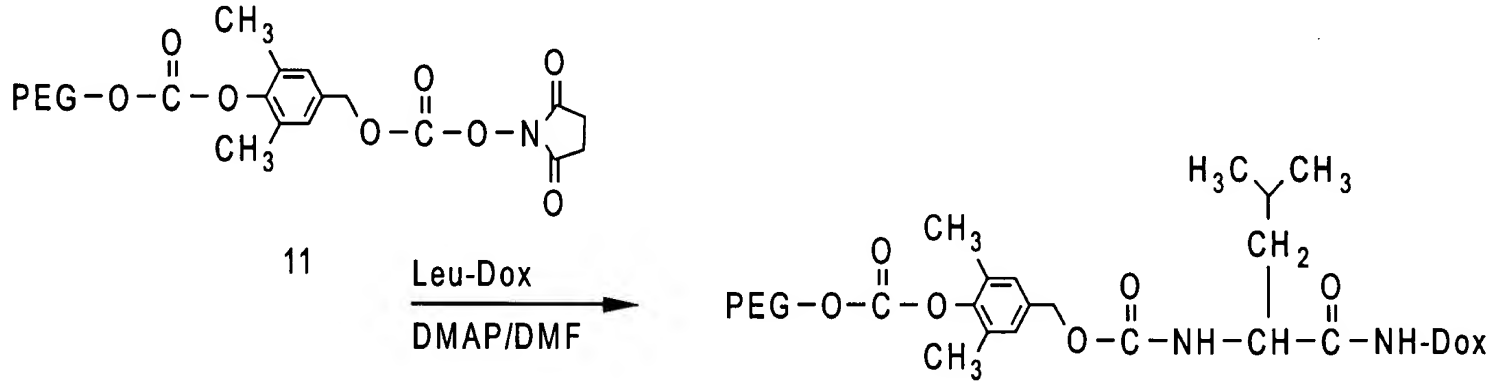
FIG. 7A



9

10

FIG. 7B



11

12

FIG. 8

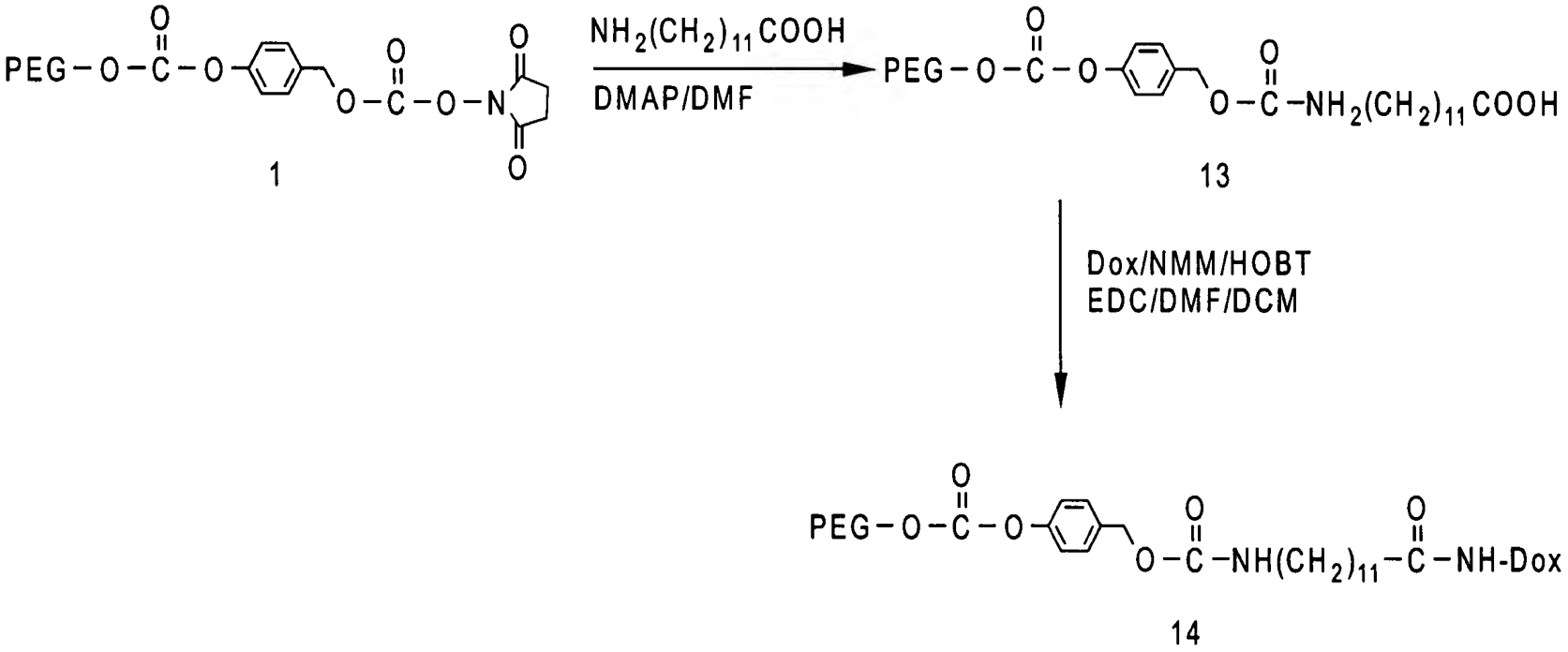
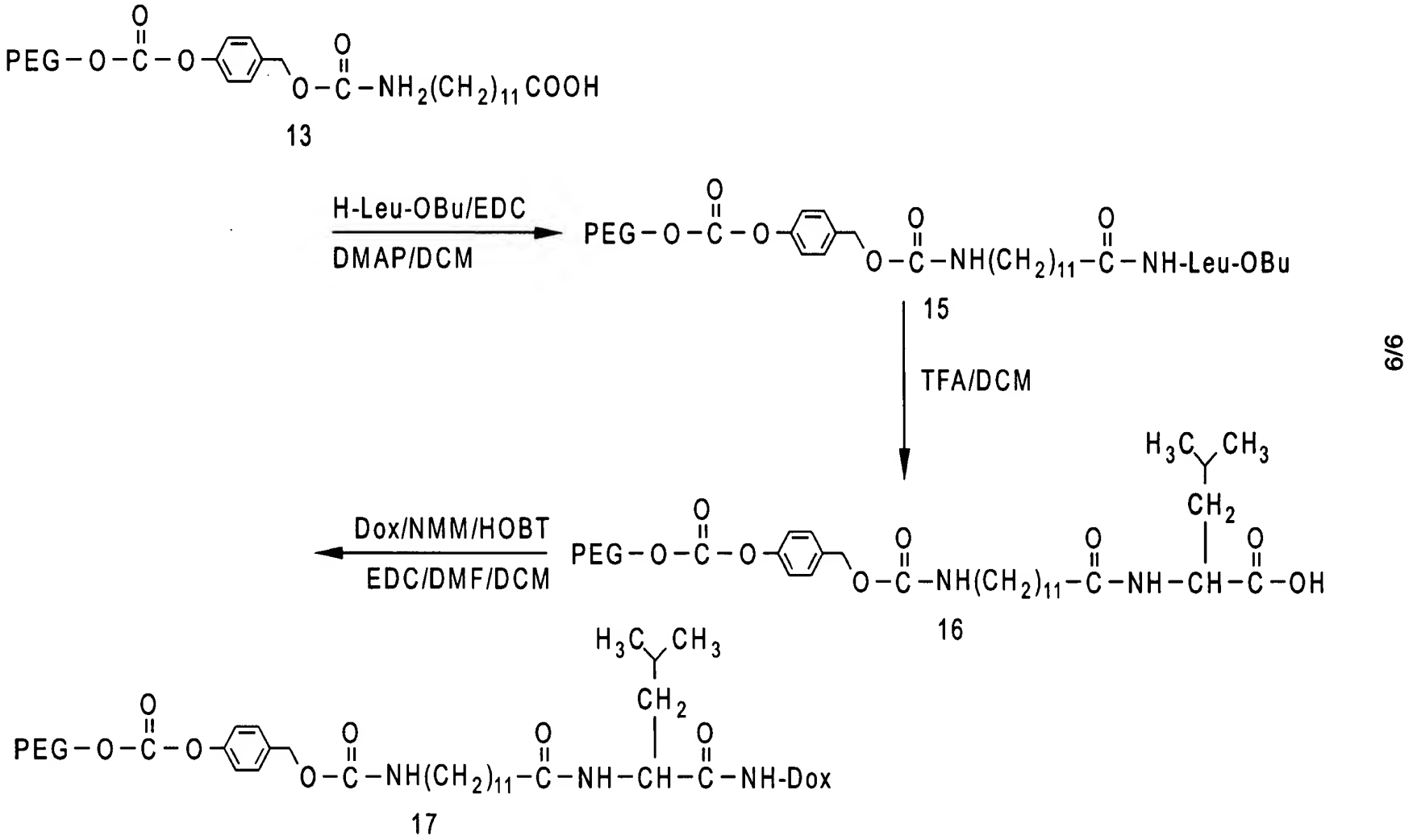

PEG-O-C-O
O-C-O-N
1
NH2(CH2)11COOH
DMAP/DMF
PEG-O-C-O
O-C-NH2(CH2)11COOH
13
Dox/NMM/HOBT
EDC/DMF/DCM
PEG-O-C-O
O-C-NH(CH2)11-C-NH-Dox
14

FIG. 9


PEG-O-C-O
O-C-NH2(CH2)11COOH
13
H-Leu-OBu/EDC
DMAP/DCM
PEG-O-C-O
O-C-NH(CH2)11-C-NH-Leu-OBu
15
TFA/DCM
H3C CH3
CH2
Dox/NMM/HOBT
EDC/DMF/DCM
PEG-O-C-O
O-C-NH(CH2)11-C-NH-CH-C-OH
16
H3C CH3
CH2
PEG-O-C-O
O-C-NH(CH2)11-C-NH-CH-C-NH-Dox
17